Recanalization of a Total Occlusion With Marked Retrograde Collateral Supply: Impact of Collateral Circulation on Fractional Flow Reserve Measurements of Donor Artery

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ABSTRACT: Fractional flow reserve (FFR)-based coronary interventions of intermediate-severity lesions are safe, cost effective, and have prognostic importance. Although FFR is not affected by heart rate or blood pressure, collateral circulation might affect FFR results. Intermediate stenosis at the donor artery might be overestimated with FFR measurement due to coronary steal. Moreover, the amount of collateral circulation might be a strong determinant of this inaccurate measurement. In this report, we present 8 patients who underwent percutaneous coronary intervention for totally or subtotally occluded recipient vessels that were collateralized by a vessel with intermediate-degree stenosis proximal to the separation of the donor side branch evaluated by quantitative coronary angiography (QCA). In patients with Rentrop grade-2 or grade-3 collateral flow, FFR value of the donor artery was increased at least 0.10 after revascularization of the recipient artery. However, FFR value did not change significantly in patients with Rentrop grade-0 or grade-1 collateral flow following revascularization. In this case series, we suggest that well-developed collateral circulation might result in overestimation of the FFR value in the donor artery with mild stenosis. Therefore, in patients undergoing intervention to the recipient artery with a well-developed collateral supply and an intermediate stenosis at the donor artery, hemodynamic significance of the stenotic lesion should be evaluated not only before but also after coronary intervention. However, if there is no sufficient collateral circulation to totally occluded arteries, FFR values of donor arteries seem to be relatively stable both before and after PCI to the recipient artery.

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Key words: total occlusion, donor coronary artery, intermediate stenosis, collateral flow, fractional flow reserve

Fractional flow reserve (FFR) is frequently used to evaluate the hemodynamic significance of coronary artery stenosis with intermediate anatomic severity. FFR-based coronary interventions of intermediate severity lesions are safe, cost effective, and have prognostic importance.[1-4] Although FFR is not affected from heart rate or blood pressure, collateral circulation might affect FFR results.[5] Intermediate stenosis at the donor artery might be overestimated with FFR measurement due to coronary steal. Moreover, the amount of collateral circulation might be a strong determinant of this inaccurate measurement. In this report, we presented 8 patients who underwent PCI for totally or subtotally occluded vessels that were collateralized by a vessel with intermediate-degree stenosis proximal to the separation of the donor side branch.

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Case Series. *Eight patients with totally or subtotally occluded coronary arteries that were supplied by collateral arteries with mild stenosis proximal to the separation of the collateral side branches were included in the study. Patients presenting with acute coronary syndromes and total occlusion of the infarct-related artery were excluded. Before the revascularization procedure, myocardial viability was detected at the occluded vessel site. Before the PCI procedure to the totally or subtotally occluded coronary artery, severity of stenosis of the donor artery was evaluated by quantitative coronary angiography (QCA) and FFR for all patients.*

The myocardium at risk distal to the total occlusion (expressed as the myocardial jeopardy index; MJI) was angiographically estimated using the modified version of the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) score, which has been previously described.[6] In brief, the left ventricle is divided into regions according to pathological studies in humans, evaluating the relative proportion of myocardium perfused by each coronary artery.[7,8] Location (proximal, mid, or distal) of the culprit lesion, vessel dominance, site of occlusion, and size of the major branches of the infarct-related artery were taken into consideration in creating a template that calculated the percentage of jeopardized myocardium for a given site of occlusion.[9]

FFR measurements were made using Volcano FFR wire (Volcano Corporation, Inc) as previously described.[10] Before each FFR measurement, calibration of the wire was performed at the tip of the catheter. Then, the wire was advanced and positioned to the distal side of the stenotic lesion, followed by a bolus of 200 µg isosorbide dinitrate to avoid any form of epicardial vasoconstriction. Maximal hyperemia was induced by 90 µg and 120 µg intracoronary adenosine for right and left coronary arteries, respectively. After measurements, the pressure wire was pulled back until the sensor was close to the tip of the guiding catheter to ensure that no drift had occurred.

After successful revascularization of the recipient arteries, FFR measurements of donor arteries were repeated as described above. If

Table 1. Demographic and angiographic properties of patients.

	Case Number	Age (years)	Sex	Totally or Subtotally Occluded Artery	Donor Artery	Percent Stenosis in Donor Artery by QCA	Rentrop Collateral Flow Grade
Group 1	Case 1	61	M	RCA	LAD	64%	3
	Case 2	51	M	LAD	RCA	55%	3
	Case 3	61	F	CX	RCA	76%	3
	Case 4	52	M	RCA	LAD	72%	2
Group 2	Case 5	59	F	LAD	RCA	53%	1
	Case 6	64	M	RCA	LAD	68%	1
	Case 7	52	M	RCA	LAD	74%	1
	Case 8	75	M	RCA	LAD	52%	0

QCA = quatitative coronary angiography; M = Male; F = Female; RCA = right coronary artery; LAD = left anterior descending coronary artery; CX = circumflex artery.

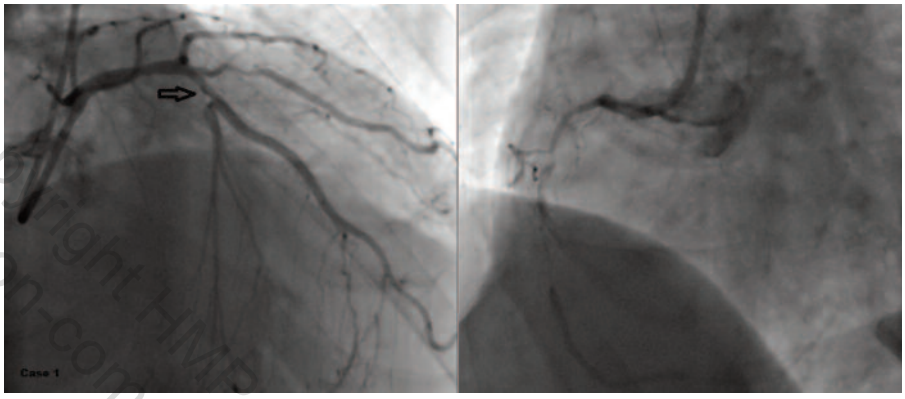

Figure 1. *A 61-year-old male hypertensive patient was admitted to our hospital with typical angina pectoris that accelerated for 2 weeks. Coronary angiography demonstrated subtotal occlusion of the right coronary artery (RCA) and a mild stenosis (arrow) at the proximal left anterior descending (LAD) artery, which gives Rentrop grade-3 collateral branches to the RCA. Initial and final fractional flow reserve values were 0.7 and 0.81, respectively.*

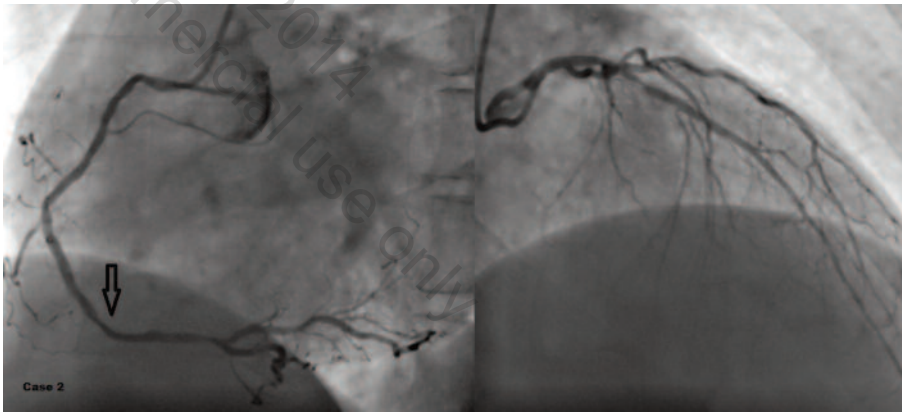

Figure 2. *A 51-year-old hypertensive male patient with history of coronary artery disease and dyslipidemia was admitted to our hospital with atypical exercise angina. Treadmill exercise test demonstrated prominent ST-segment depression through the anterior leads. Coronary angiography revealed subtotal restenosis of the left anterior descending stent and intermediate stenosis (arrow) at the right coronary artery before giving rise to the posterior descending artery. Initial and final FFR values were 0.63 and 0.86, respectively.*

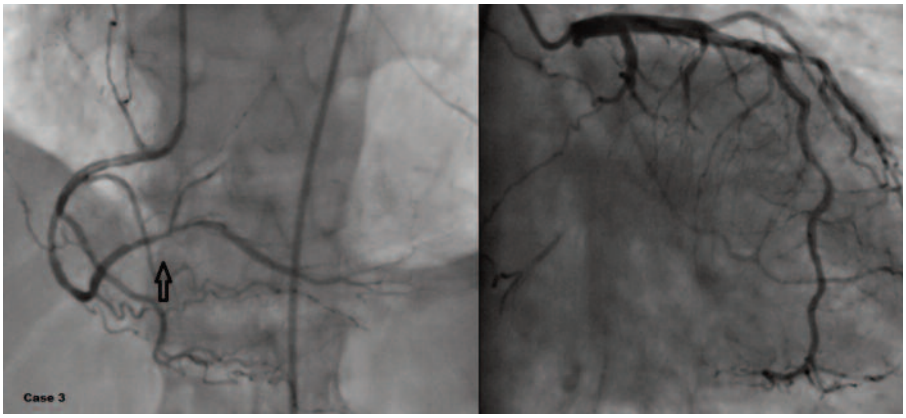

Figure 3. *A 61-year-old female patient was admitted to our hospital with complaints of typical chest pain and dyspnea for 20 days. She had history of hypertension, diabetes mellitus, chronic obstructive pulmonary disease, and myocardial infarction. Stress echocardiography revealed biphasic response to accelerated dobutamine doses suggesting viability. Coronary angiography revealed total occlusion of the CX and intermediate stenosis at the RCA (arrow) with Rentrop grade-3 collateral flow to the CX. Initial and final FFR values were 0.62 and 0.72, respectively.*

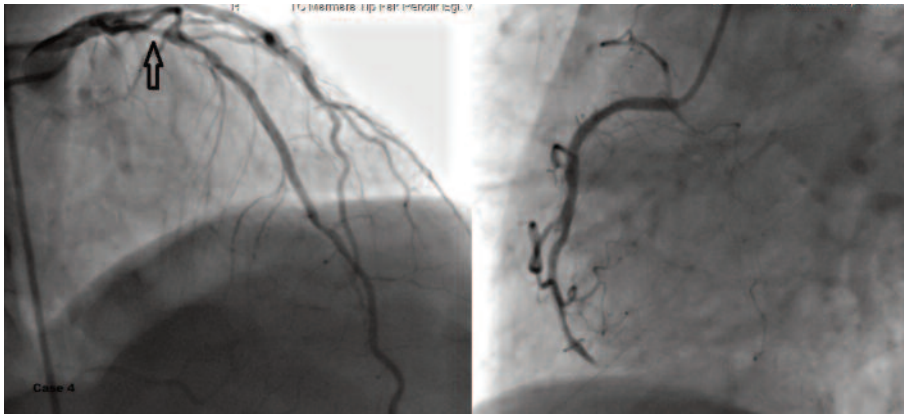

Figure 4. *A 52-year-old male with a history of diabetes mellitus for 5 years admitted to our hospital. Echocardiographic examination revealed left ventricular wall-motion abnormality in the inferior segments. Myocardial perfusion scintigraphy examination demonstrated reversible ischemia and infarct at the inferior wall. Total occlusion at the mid-level of the RCA with well-developed collateral supply from the LAD with an intermediate proximal stenosis (arrow) was detected by coronary angiography. Initial and final FFR values were 0.68 and 0.78, respectively.*

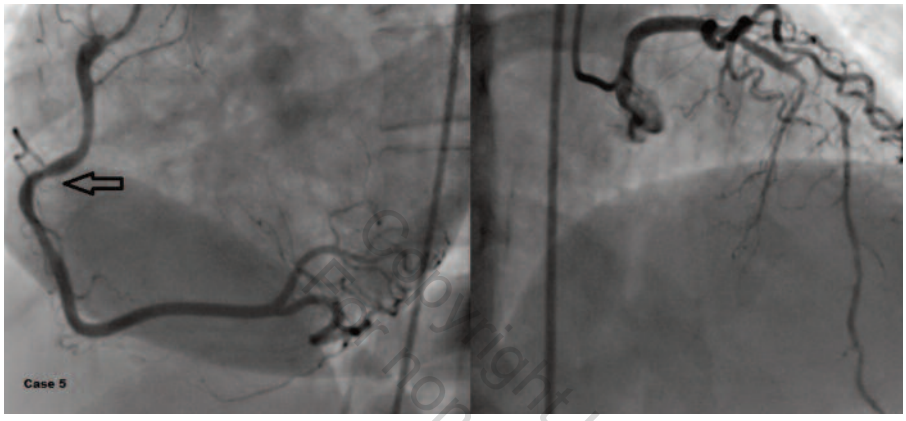

Figure 5. *A 59-year-old female was admitted to our hospital with typical chest pain for 1 month. She had hypertension for 3 years and a 20 pack-year smoking history. Before coronary angiography, myocardial perfusion scintigraphy examination revealed reversible ischemia at the mid and apical levels of the anterior left ventricular wall. Coronary angiography demonstrated a subtotally occluded mid LAD lesion and an intermediate stenosis of proximal RCA (arrow) giving poor collateral circulation to the LAD. Initial and final FFR values were 0.84 and 0.88, respectively.*

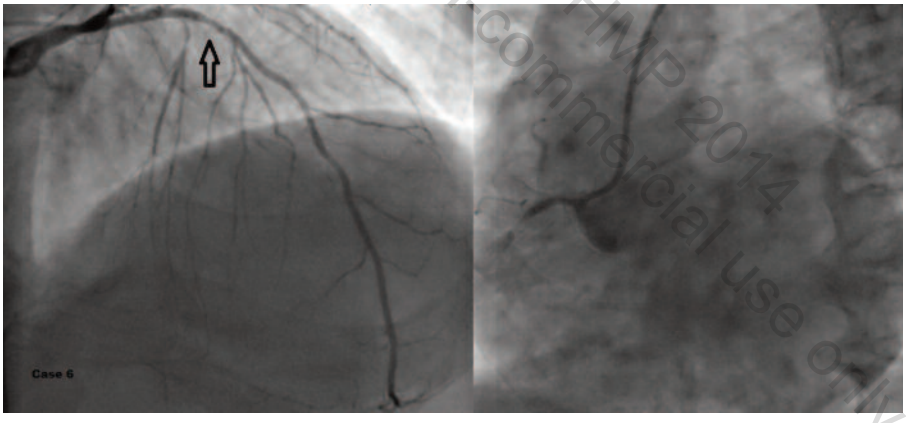

Figure 6. *A 64-year-old male with history of diabetes mellitus and 30 pack-years of smoking was admitted to our hospital with typical chest pain for 6 months despite optimal medical treatment. Coronary angiography revealed total occlusion of the right coronary artery (RCA) and intermediate severity stenosis at the left anterior descending (LAD; arrow) with Rentrop grade-1 collateral flow from the LAD to the RCA. Initial and final fractional flow reserve values were 0.65 and 0.67, respectively.*

final FFR value was less than 0.8, PCI was also planned for the donor artery. Collateral flow was graded according to Rentrop classification from 0 to 3. Patients were then divided into two groups according to Rentrop grade (group 1 = Rentrop grade 2 or grade 3; group 2 = Rentrop grade 0 or grade 1). Data are presented as median (min-max) and pre- and postprocedural FFR values were compared by two related sample tests (Wilcoxon). Postprocedural difference in FFR values, mean QCA values, and ages were compared using Mann-Whitney U-test.

Results. Patient demographics are presented in Table 1. Six male and 2 female patients were evaluated. Initial coronary angiograms of the 8 patients are shown in corresponding Figure 1 to 8. Four patients were found in group 1 (Rentrop grade 2 or 3) and 4 patients were found in group 2 (Rentrop grade 0 or 1). Mean age was 57 years (range, 51-67 years) in group 1 and 62.5 years (range, 53-75 years) in group 2 (*P*=.38). The PCI procedure was successfully performed to the right coronary artery (RCA) in 5 cases, circumflex (CX) artery in 1 case, and left anterior descending (LAD) coronary artery in 2 cases.

FFR measurements of the donor arteries before and after PCI and MJI are presented in Table 2 and Figure 9. Median FFR measurements increased after successful PCI in group 1 (0.65 [min-max, 0.62-0.70] vs 0.79 [min-max, 0.72-0.86]; *P*=.05). However, median FFR measurements remained stable despite successful recipient artery PCI in group 2 (0.77 [min-max, 0.65-0.89] vs 0.78 [min-max, 0.67-0.88]; *P*=.58). Mean increase in FFR value in group 1 was statistically significant compared with group 2 (0.135 vs 0.007; *P*=.02).

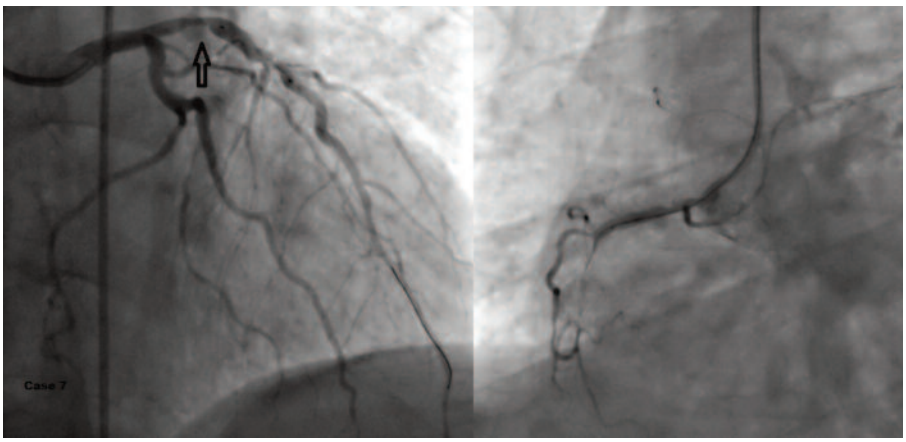

Figure 7. *A 52-year-old male with a history of smoking was admitted with acute-onset chest pain and transient ST-segment elevation at the inferior leads. Coronary angiography was followed with a successful primary PCI and stent to the CX. Intermediate stenosis at the mid LAD (arrow) and total occlusion of the RCA were also detected. The distal portion of the RCA was supplied by the LAD, with Rentrop grade-1 collateral flow. Revascularization of the RCA total occlusion was performed after 6 days of myocardial infarction. Initial and final FFR values of the LAD stenosis were 0.71 and 0.69, respectively.*

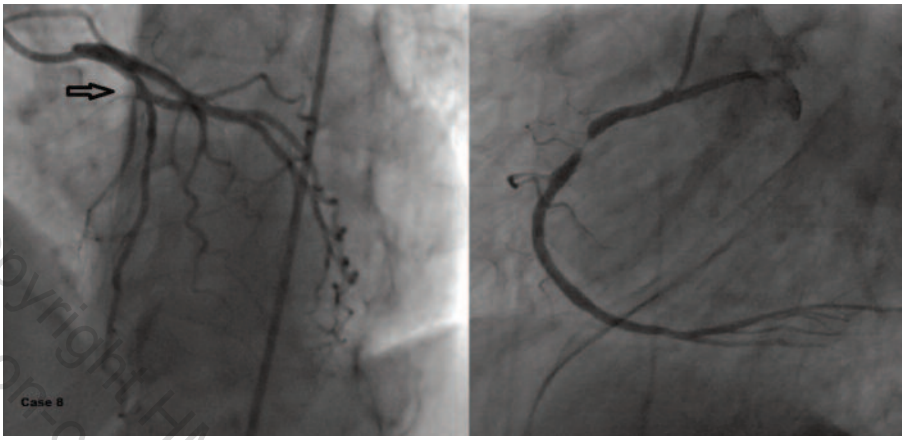

Figure 8. *A 75-year-old male was admitted to our hospital with complaints of exercise dyspnea and typical chest pain for 2 months. He had history of diabetes mellitus, hypertension, atrial fibrillation, and 25 pack-years of smoking. Coronary angiography demonstrated subtotal occlusion of the right coronary artery and intermediate severity stenosis of the left anterior descending, with Rentrop grade-0 collateral flow. Initial and final fractional flow reserve values were 0.89 and 0.88, respectively.*

Severity of stenosis in the donor arteries was also evaluated by QCA. There was no significant difference in severity between groups (median severity, 68% [range, 55%-76%] in group 1 vs 60.5% [range, 52%-74%] in group 2; *P*=.38). Myocardial jeopardy index of the two groups was also similar (19.87% in group 1 vs 15.25% in group 2; *P*=.30).

Discussion. In our case series, FFR results of donor arteries changed after revascularization of the recipient arteries, especially in patients with Rentrop grade-2 or grade-3 collateral flow and mild anatomic stenosis detected by QCA. FFR values increased at least 0.10 in patients with Rentrop grade-2 or grade-3 collateral circulation after the revascularization procedure. However, FFR value did not change significantly in patients with Rentrop grade-0 or grade-1 collateral flow and high percent stenosis by QCA. We think the effect of coronary steal on the donor artery was minimal due to poorly developed collateral circulation and ischemia was prominent because of high-grade anatomic occlusion. In the literature, there were only a few case reports showing increase in FFR value of the donor artery following PCI to the recipient artery.[11-13] A previous report of a patient with well-developed collateral circulation from the donor artery revealed an increase in the FFR value from 0.84 to 0.96 after PCI to the recipient artery.[11] However, another report of a patient with a mild LAD stenosis revealed no alteration in FFR value after surgical revascularization of occluded RCA and CX arteries.[14]

Collateral circulation is an important alternative source of blood supply to the jeopardized myocardium of critically occluded arteries. Well-developed collateral circulation might help to sustain viability and contractility at the ischemic myocardial tissue.[15,16] Extensive amounts of myocardium that is perfused by collateral circulation might provoke myocardial ischemia at the donor artery region by coronary steal syndrome. However, poor collateral circulation or small areas at ischemic risk might not result in an evident blood shift to the recipient artery. We also detected stable FFR results in patients with poor collaterals despite similar MJI, supporting this hypothesis.

Although FFR is not affected by heart rate, contractility, or blood pressure,[17] in case of an intermediate-degree stenosis determined by QCA in the donor coronary artery, hemodynamic evaluation of the occlusion by FFR might overestimate the severity due to collateral blood flow. However, if the stenosis demonstrated by QCA is severe, FFR measurement seems more reliable independent of the collateral circulation. FFR results are restrictive for donor artery interventions in order to augment coronary blood flow to both the donor and recipient myocardia in conditions in which there is no chance of revascularization of totally occluded recipient artery.

Myocardial jeopardy index was successfully used to estimate the amount of myocardium at risk in patients presenting with myocardial infarction.[9] However, there was no relation between MJI and FFR measurements in our patient

Table 2. Fractional flow reserve results of the donor artery before and after revascularization of the recipient artery.

	Case Number	Before PCI		After PCI		Myocardial Jeopary Index
		Basal	After Adenosine	Basal	After Adenosine	
Group 1	Case 1	0.83	0.70	0.84	0.81	21.25%
	Case 2	0.82	0.63	0.93	0.86	27.50%
	Case 3	0.62	*	0.72	*	18.50%
	Case 4	0.84	0.68	0.86	0.78	15.25%
Group 2	Case 5	0.91	0.84	0.96	0.88	27.50%
	Case 6	0.75	0.65	0.77	0.67	15.25%
	Case 7	0.84	0.71	0.88	0.69	9.25%
	Case 8	0.94	0.89	0.95	0.88	15.25%

*Because basal hemodynamic value demonstrated significant stenosis, intracoronary adenosine was not applied.

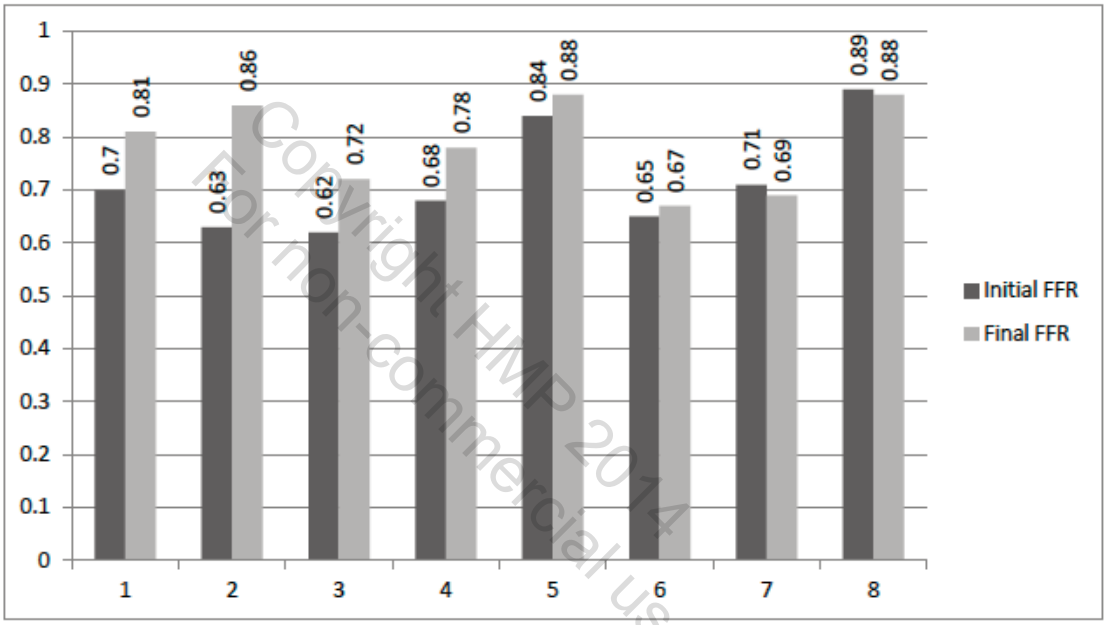

Figure 9. *Fractional flow reserve values of cases before and after percutaneous coronary intervention procedure. Cases 1, 2, 3, and 4 are included in group 1; the remaining cases are in group 2.*

group. Myocardial jeopardy index is highly dependent to the occluded vessel and most of our patients presented with RCA occlusions. There were only 2 patients with LAD occlusions and high amounts of myocardium at risk. This might have affected the results of our study. Further large-scale studies with equal distribution of the occluded vessels might clarify our results.

To date, there is no clinical study evaluating the effect of collateral circulation on FFR value of donor arteries after revascularization of the recipient artery. In this case series, despite an insufficient number of patients, we suggest that well-developed collateral circulation might cause overestimation of the FFR value in the donor artery with intermediate-degree stenosis. Therefore, in patients undergoing intervention for the recipient artery with a well-developed collateral and intermediate stenosis at the donor artery, hemodynamic significance of stenotic lesion should be evaluated not only before but also after coronary intervention. However, if there is no sufficient collateral circulation to the totally occluded recipient arteries, FFR values of donor arteries seem to be relatively stable both before and after PCI to the recipient artery. In addition to QCA, intravascular ultrasound and coronary computed tomography angiography might also be used as supporting modalities to define the anatomic severity of the donor artery occlusions.

In patients with an occluded coronary artery that was supplied by a well-developed retrograde collateral vessel, anatomic significance and localization of the donor artery lesion (distal or proximal to the septal collaterals in the LAD), intensity of the collateral flow, dominance of the recipient artery, MJI of the occluded vessel, existence of stenotic lesions distal to the total occlusion site, presence of unnoticed epicardial or atrial collaterals, and elevated left ventricular end-diastolic pressure

might affect the hemodynamic significance of the stenotic lesion at the donor artery. Hemodynamic evaluation should be repeated after successful revascularization of the recipient artery, which might minimize the coronary steal syndrome. However, in case of insufficient collateral circulation to the totally occluded recipient arteries, repeated FFR measurement of donor arteries seems unnecessary. These data might help to reduce unnecessary donor artery interventions and surgical referrals, which will preclude the potential complications of these procedures.

Study limitations. In this case series, an insufficient number of patients was the main limitation that might affect the statistical analysis results. To increase the reliability of our results, new studies with a sufficient number of patients should be planned. Although patients presenting with acute coronary syndromes were excluded in our study, many patients with totally occluded vessels and retrogradely supplied collaterals undergo revascularization procedures during daily clinical practice. Our results require validation in patients with acute coronary syndrome.

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